

Attorney Docket No. 9233-62

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor: Ekwuribe et al.

Confirmation No.: 2357

Serial No.: 09/873,757

Art Unit: 1654

Filed: June 4, 2001

Examiner: J. Russel

For: *Mixtures of Growth Hormone Drug-Oligomer Conjugates Comprising Polyalkylene Glycol, Uses Thereof, and Methods of Making Same*

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

January 13, 2004

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Sir:

Attached is a list of documents on Form PTO-1449, along with a copy of each listed document. It is requested that these documents be considered by the Examiner and officially made of record in accordance with the provisions of 37 C.F.R. § 1.97 and Section 609 of the MPEP.

Also attached is a Declaration of James Gordon Still under 37 C.F.R. § 1.132 (originally prepared for submission in application serial no. 10/075,097) in which Dr. Still provides information about the slides that are included on the attached PTO Form 1449 as items 99 and 103. Although applicants provide these slides to the examiner in the interest of full disclosure in accordance with applicant's duty, it is applicants' belief that these slides are not "printed publications" as set forth in 35 U.S.C. § 102(b) and are thus not prior art to the claimed invention. Applicants base this belief on a comparison of the facts in this case as set forth in Dr. Still's Declaration with the facts set forth in *Regents of the University of California v. Howmedica, Inc.* [210 U.S.P.Q. 727 (D.N.J. 1981); *aff'd*, 676 F.2d 687 (3rd Cir. 1982); copy enclosed], in which the court determined that slides shown during an oral presentation did not constitute a "printed publication" within the meaning of 35 U.S.C. § 102(b). Because the facts reviewed by the court parallel the facts of the present application, applicants believe these slides are not prior art against the invention as claimed in the present application.

This Supplemental Information Disclosure Statement and Form PTO-1449 are submitted in accordance with 37 C.F.R. § 1.97(b)(4), before the mailing of a first Office

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Action after the filing of a Request for Continued Examination. Therefore, no fee is believed due. However, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220

Respectfully submitted,



Shawna Cannon Lemon
Registration No. 53,888

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Susan E. Freedman

Date of Signature: January 13, 2004

Substitute form 1449A/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application Number	09/873,757
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				First Named Inventor	Nnochiri N. Ekwuribe
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				Examiner Name	J. Russel
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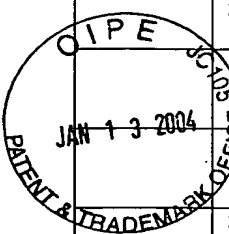
FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY
		Office	Number	Kind Code (if known)		
	1	EP	0 822 218	A2	Glenn A. Miller et al.	02/04/1998
	2	JP	01207320		Daicel Chem Ind Ltd.	08/21/1989
	3	EP	0 483 465	B1	Salama et al.	08/02/1995
	4	EP	0 511 903	A2	Medgenix Group, S.A.	11/04/1992
	5	DE	196 32 440	A1	BASF AG	02/19/1998
	6	EP	0 031 567	A2	Takeda Yakuhin Kogyo Kabushiki Kaisha	07/08/1981
	7	EP	0 597 007	B1	Smithkline Beecham Corporation	10/16/1996
	8	EP	0 621 777	B1	Alfatec-Pharma GmbH	09/11/1996
	9	EP	0 797 615	B1	The University of Nottingham	01/13/1999
	10	GB	1 492 997		Derek George Smyth	11/13/1977
	11	JP	1 254 699		Kodama Co., Ltd.	10/11/1989
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	13	WO	93/01802		Debio Recherche Pharmaceutique, S.A.	02/04/1993
	14	WO	95/09831		Piero Del Soldato et al.	04/13/1995
	15	WO	95/30641		Nicox Limited	11/16/1995
	16	WO	98/07745		Micrologix Biotech, Inc.	02/26/1998
	17	WO	99/65941	A1	King College London et al.	12/23/1999
	18	WO	99/32134		Enzon Inc.	07/01/1999

OTHER NON PATENT LITERATURE DOCUMENTS				T
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published		
	19	Abuchowski, A. and F. F. Davis "Soluble Polymer-Enzyme Adducts" pp. 367-383, <i>Enzymes as Drugs</i> , Ed. J. S. Holcenberg, John Wiley (1981)		
	20	Agarwal et al. "Polymethacrylate-based Microparticulates of Insulin for Oral Delivery: Preparation and In Vitro Dissolution Stability in the Presence of Enzyme Inhibitors" <i>International Journal of Pharmaceutics</i> 225:31-39 (2001)		
	21	Akiyama et al. "The Synthesis of New Derivatives of 1-β-D-Arabinofuranosylcytosine" <i>Chem. Pharm. Bull.</i> 26(3):981-984 (1978)		
	22	Allaudeen et al. "Orally Active Insulin: A Single Insulin Conjugate Selected for Future Studies" 60th Annual Meeting of the American Diabetes Assoc., Atlanta, GA, June 2000 (Abstract)		
	23	Anderson et al. "HIM2, a Novel Modified Insulin, has Improved Systemic Pharmacokinetics in Normal Dogs, Compared to Unmodified Insulin" American Diabetes Association 62nd Annual Meeting, June 2002 (Abstract)		
	24	Ansell et al. "Application of Oligo-(14-amino-3,6,9,12-tetraoxatetradecanoic acid) Lipid Conjugates as Steric Barrier Molecules in Liposomal Formulations" <i>Bioconjugate Chem.</i> 10:653-666 (1999)		
	25	Aoshima et al. "N ⁴ -Behenoyl-1-β-D-Arabinofuranosylcytosine as a Potential New Antitumor Agent" <i>Cancer Research</i> 37:2481-2486 (1977)		
	26	Baker, D. C. et al. "Prodrugs of 9-β-D-Arabinofuranosyladenine. 1. Synthesis and Evaluation of Some 5'-(O-Acyl) Derivatives" <i>J. Med. Chem.</i> 21(12):1218-1221 (1978)		
	27	Banting et al. "Pancreatic Extracts in the Treatment of Diabetes Mellitus: Preliminary Report" <i>Can. Med. Assoc. J.</i> 145(10):1281-1286 (1991)		
	28	Baudys et al. "Stabilization and Intestinal Absorption of Human Calcitonin" <i>J. Contr. Rel.</i> 39:145-51 (1996)		
	29	Baudys et al. "Synthesis and Characterization of Different Glycosylated Derivatives of Insulin" <i>Proceed. Intern. Symp. Cont. Rel. Bioactive. Mater.</i> 19:210-211 (1992)		
	30	Block, Lawrence H. "Pharmaceutical Emulsions and Microemulsions" <i>Pharmaceutical Dosage Forms: Disperse Systems</i> Vol. 2, Ed. Lieberman et al., pp. 47-109 (1996)		

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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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			Examiner Name	J. Russel	
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	31	Boccu et al. "Pharmacokinetic Properties of Polyethylene Glycol Derivatized Superoxide Dismutase" <i>Pharm. Res. Comm.</i> 14:113-120 (1982)	
	32	Bone et al. "Successful Treatment of an Insulin Dependent Rat Model of Human Type I Diabetes with Orally Active Insulin" Program and Abstracts, 4th International Workshop on Lessons from Animal Diabetes, Omiya, Japan, November 1994 (Abstract)	
	33	Bone et al. "Successful Treatment of Type 1 Diabetes with Orally-Active Insulin: Studies in The Insulin Dependent BB/S Rat" Program and Abstracts, 55th Annual Meeting of the American Diabetes Association, Atlanta Georgia, June 1995 (Abstract)	
	34	Brange and Volund "Insulin Analogs with Improved Pharmacokinetic Profiles" <i>Advanced Drug Delivery Reviews</i> 35:307-335 (1999)	
	35	Brange et al. "Chemical Stability of Insulin. 1. Hydrolytic Degradation During Storage of Pharmaceutical Preparations" <i>Pharm. Res.</i> 9(6):715-726 (1992)	
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	38	Chien, Y. W., <i>Novel Drug Delivery Systems</i> , pp. 678-679, Marcell Deffer, Inc., New York, N.Y. (1992)	
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	40	Clement et al. "Effects of Multiple Doses of Orally Administered Hexyl Insulin M2 (HIM2) on Postprandial Blood Glucose (PPG) Concentrations in Type 1 Diabetic (T1) Patients" American Diabetes Association 62nd Annual Meeting, June 2002 (Poster)	
	41	Clement et al. "Oral Insulin Product Hexyl-Insulin Monoconjugate 2 (HIM2) in Type 1 Diabetes Mellitus: The Glucose Stabilization Effects of HIM2" <i>Diabetes Technology & Therapeutics</i> 4(4):459-466 (2002)	
	42	Clement, Stephen "A Dose-Escalation Study of the Effects of Two Sequential Doses of Oral Modified Insulin on Blood Glucose Concentrations in Patients with Type 1 Diabetes Mellitus" American Diabetes Association Annual Meeting (June 25, 2001) (Abstract)	
	43	Clement, Stephen "A Dose-Escalation Study of the Effects of Two Sequential Doses of Oral Modified Insulin on Blood Glucose Concentrations in Patients with Type 1 Diabetes Mellitus" American Diabetes Association Annual Meeting (June 25, 2001) (Poster)	
	44	Conradi et al. "The Influence of Peptide Structure on Transport Across Caco-2 Cells" <i>Pharm. Res.</i> 8(12):1453-1459 (1991)	
	45	Coombes et al. "Biodegradable Polymeric Microparticles for Drug Delivery and Vaccine Formulation: the Surface Attachment of Hydrophilic Species Using the Concept of Poly(Ethylene Glycol) Anchoring Segments" <i>Biomaterials</i> 18:1153-1161 (1997)	
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48	Delgado et al. "The Uses and Properties of PEG-Linked Proteins" <i>Critical Reviews in Therapeutic Drug Carrier Systems</i> 9(3,4):249-304 (1992)		
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50	Engel et al. "Insulin: Intestinal Absorption as Water-in-Oil-in-Water Emulsions" <i>Nature</i> 219:856-857 (1968)		
51	Fasano, A. "Innovative strategies for the oral delivery of drugs and peptides" <i>TIBTECH</i> 16:152-157 (1998)		
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57	Hashimoto et al. "Synthesis of Palmitoyl Derivatives of Insulin and Their Biological Activities" <i>Pharmaceutical Research</i> 6(2):171-176 (1989)	
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68	Krishnan, B. Radha, et al., "Stability and Physical Characteristics of Orally Active Amphiphilic Human Insulin Analog, Methoxy (Polyethylene Glycol) Hexanoyl Human Recombinant Insulin (HIM2)", <i>Proceed. Int'l. Symp. Control. Rel. Bioact. Mater.</i> , 27:1038-1039 (2000)	
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71	Maislos et al. "The Source of the Circulating Aggregate of Insulin in Type I Diabetic Patients is Therapeutic Insulin" <i>J. Clin. Invest.</i> 77:717-723 (1986)	
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82	Price, JC <i>Polyethylene Glycol</i> , pp. 355-361	
83	Puskas et al. "Investigation of Chymotrypsin Digestion Profile of Orally Active Insulin Conjugate HIM2" <i>AAPS Pharm Sci.</i> 3(3) 2001 (Abstract)	
84	Radhakrishnan et al. "Chemical Modification of Insulin with Amphiphilic Polymers Improves Intestinal Delivery," <i>Proceed. Intl. Symp. Control. Rel. Bioact. Mater.</i> 25:124-125 (1998) (Abstract)	

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	85	Radhakrishnan et al. "Oral Delivery of Insulin: Single Selective Modification at B29-LYS With Amphiphilic Oligomer" Program and Abstracts, 1999 National Meeting of the Ameri. Assoc. Pharm. Scient., New Orleans, LA (1999) (Abstract)	
	86	Radhakrishnan et al. "Structure-Activity Relationship of Insulin Modified with Amphiphilic Polymers" Program and Abstracts, 1998 National Meeting of the Amer. Assoc. Pharm. Scient., San Francisco, CA Pharm. Sci. 1(1):S-59 (1998) (Abstract)	
	87	Ratner, R. E. et al. "Persistent Cutaneous Insulin Allergy Resulting from High-Molecular Weight Insulin Aggregates" <i>Diabetes</i> 39:728-733 (1990)	
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	94	Shah and Shen "Transcellular Delivery of an Insulin-Transferrin Conjugate in Enterocyte-like Caco-2 Cells" <i>Journal of Pharmaceutical Sciences</i> 85(12):1306-1311 (1996)	
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	98	Still and McAllister "Effects of Orally Active Modified Insulin in Type 1 Diabetic Patients" <i>Clinical Pharmacol. Therap.</i> 69(2):P95 (Feb. 2001) (Abstract)	
	99	Still and McAllister "Effects of Orally Active Modified Insulin in Type I Diabetic Patients" Slide Presentation Annual Meeting of the American Society for Clinical Pharmacology & Therapeutics, Orlando, FL, March 9, 2001	
	100	Still and McAllister "Effects of Orally Active Modified Insulin in Type I Diabetic Patients" Annual Meeting of the American Society for Clinical Pharmacology & Therapeutics, Orlando, FL, March 9, 2001 (Handout)	
	101	Still et al. "Magnitude and Variability of Pharmacokinetic and Glucodynamic Responses to Modified Human Insulin Administered Orally to Healthy Volunteers" <i>Diabetes Research and Clinical Practice</i> 56:S77 (2002)	
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